Biochips Containing Arrays of Carbon-Nanotube Electrodes

Small quantities of biomarkers could be detected rapidly, with simplified preparation.

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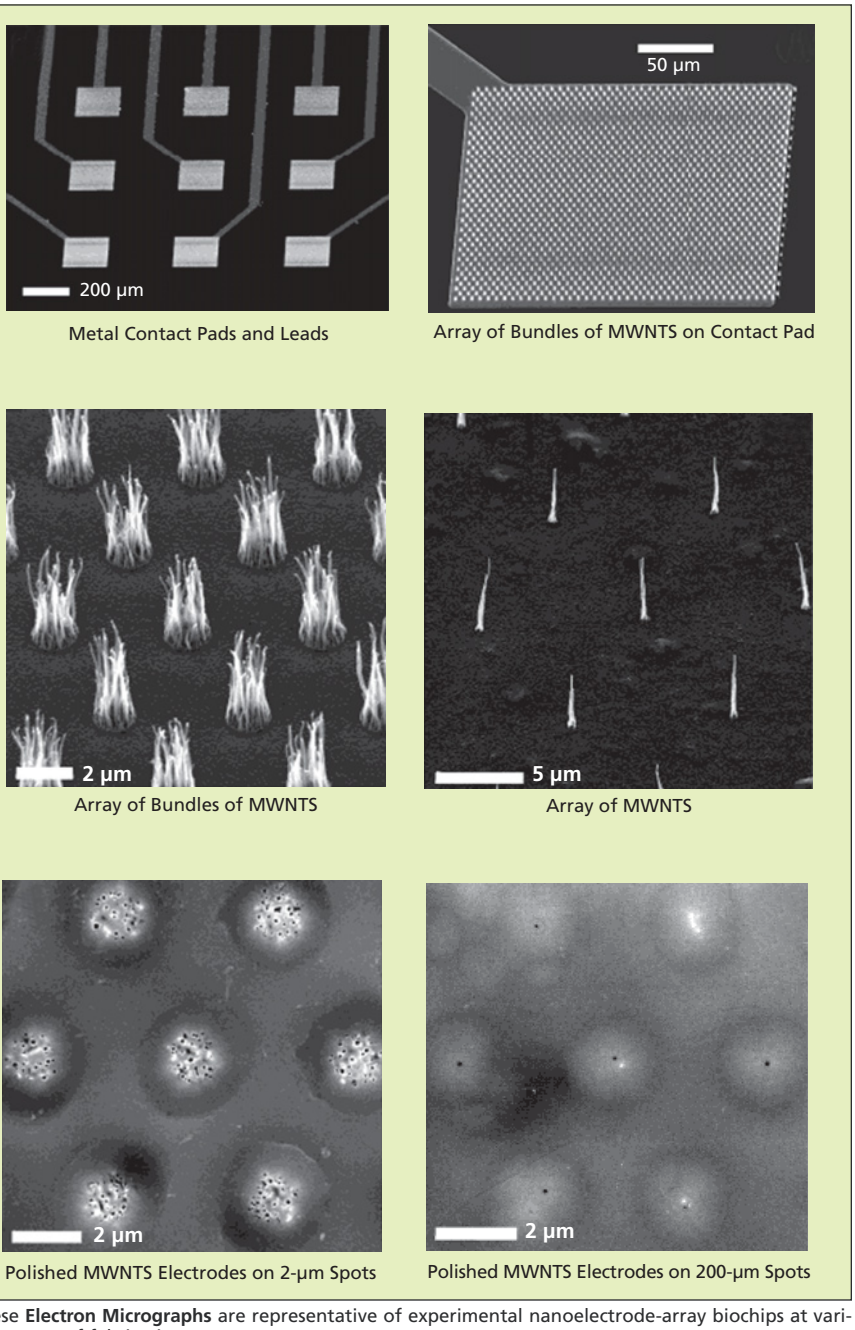
Biochips containing arrays of nanoelectrodes based on multiwalled carbon nanotubes (MWCNTs) are being developed as means of ultrasensitive electrochemical detection of specific deoxyribonucleic acid (DNA) and messenger ribonucleic acid (mRNA) biomarkers for purposes of medical diagnosis and bioenvironmental monitoring. In mass production, these biochips could be relatively inexpensive (hence, disposable). These biochips would be integrated with computer-controlled microfluidic and microelectronic devices in automated hand-held and bench-top instruments that could be used to perform rapid *in vitro* genetic analyses with simplified preparation of samples.

Carbon nanotubes are attractive for use as nanoelectrodes for detection of biomolecules because of their nanoscale dimensions and their chemical properties.

- In general, as the size of an electrode is reduced, the signal-to-noise ratio (hence, the sensitivity) and the temporal resolution obtainable in the use of the electrode increase. Of course, the nanoscale dimensions of carbon nanotubes are favorable for miniaturization.
- MWCNTs having large length-to-diameter ratios, standing on metal contact pads, can readily be fabricated at wafer scale to form well-defined nanoelectrode arrays.
- MWCNTs have a wide potential window and well-defined surface functional groups, and have a high degree of biocompatibility — properties that are attractive for biosensor applications.

A biochip according to this concept includes a planar array of metal electrode contact pads and leads embedded in a dielectric substrate that typically consists of SiO_2. A single MWCNT, a bundle of MWCNTs, or an array of single MWCNTs or bundles thereof oriented perpendicular to the plane is attached to each contact pad and is long enough to lie flush with (or protrude slightly from) the outer surface of the dielectric (see figure). The exposed tips of the MWCNTs are covalently functionalized with such biomolecular probe substances as oligonucleotides, peptides, proteins, ligands, and/or enzymes chosen to interact with specific target biomolecules. In a typical envisioned application, the binding of the target molecules with the probe molecules and/or



These **Electron Micrographs** are representative of experimental nanoelectrode-array biochips at various stages of fabrication.

the products of enzyme-catalyzed chemical reactions would be detected by electrochemical methods. It is important to emphasize that unlike in some prior detection methods, time-consuming fluorescence labeling of target DNA would be unnecessary because the electrochemical signals associated with the bound target molecules can be directly electronically measured.

The fabrication of a biochip containing such an array of functionalized nanoelectrodes begins with the prefabrication of the metal electrode contact pads and leads on a SiO_2 covered silicon substrate. The MWCNTs are formed on the prefabricated contact pads by wafer-scale plasma enhanced chemical vapor deposition. In a second chemical-vapor-deposition process, the contact pads and the MWCNTs are encapsulated in SiO_2. Then by chemical mechanical polishing, SiO_2 is removed to a depth sufficient to form a planar SiO_2 outer surface with the exposed tips of the MWCNTs constituting an array of inlaid nanodisk electrodes.

In development work thus far, electrical and electrochemical properties of embedded arrays of MWCNT nanoelectrodes have been thoroughly characterized. Nanoelectrodes have been covalently functionalized with probe molecules through formation of amide bonds at exposed end of MWCNTs. Direct electrochemical detection of oxidation signals of inherent guanine bases in target nucleic acids has been demonstrated. It has been shown that fewer than 1,000 DNA or mRNA targets for each biomarker can be directly detected, making it possible to measure mRNA without amplification by polymerase chain reaction.

This work was done by Jun Li, M. Meyyappan, and Jessica Koehne of Ames Research Center, Alan Cassell of UASRC, and Hua Chen of ELORET Corp. Further information is contained in a TSP (see page 1).

This invention is owned by NASA and a patent application has been filed. Inquiries concerning rights for the commercial use of this invention should be addressed to the Ames Technology Partnerships Division at (650) 604-2954. Refer to ARC-15205-1.